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PAT 485-2 US

"a receptor or capture molecule" (page 28), an "immobilized binding molecule" (page 33) and "a binding molecule (page 34), and no new matter has been added.

Yours very truly

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Encl.

1.1 copy of each of pages 28, 33 and 34 showing proposed amendments

2.1 copy of each of pages 28, 33 and 34 showing amendments made

concentration of chemical species within the reaction zone 6 may be probed by a variety of techniques well known in the art including by optical absorbance, by luminescence or laser induced fluorescence of luminescent or fluorescent molecules or labels in the reaction zone 6 by optical detector 11 (not illustrated) or by electrochemical detection using electrochemical probe electrode(s) 7d. The reaction zone 6 may be the same composition as the hydrophilic matrix conductor 2, as in the electrophoretic separation application of this device described later. In other applications of the micro-analytical system, reaction zone 6 may be a different composition. For example in the ligand-binding assay application of the micro-analytical system reaction zone 6 contains reagents that bind with species being transported along conductor 2. Referring to the B-B' cross-section of FIG. 5C, in operation a portion of the top surface of the device is immersed in an aqueous medium. Water 50 is transported as vapor through the water vapor-permeable cover layer 3 into the initially dry, inactive hydrophilic-solid matrix conductors 2 and 2d, reservoirs 2a, 2b and 2c, and reaction or separation zone 6. The cover layer 3 is otherwise insulating, that is, it does not transport other solute species, ions or electrons.

One use of the micro-analytical system of FIG.5 is in a ligand-binding assay. In this application an electrolyte solution containing the target molecule to be assayed is introduced into the hydrophilic-matrix conductor 2 through orifice 4. This is achieved by electrokinetic pumping when a positive voltage is applied to the electrolyte solution by integral electrode 7e relative to the voltage of waste reservoir 2b applied through electrode 7b. Thus, sample solution is pumped through 2 to zone 6 which contains an immobilized [ligand] receptor or capture molecule that binds the target molecule. The bound target molecule may be detected within zone 6. A typical detection strategy known in the art is to introduce a label molecule that also binds to the target molecule. The label molecule will traverse the conductor 2 to zone 6 where it binds to the target

electrokinetic circuits and components according to this invention used in additional analytical applications include but are not limited to: devices with reaction zones incorporating pcr reactions, devices with reaction zones supporting primer extension reactions in general, devices with reaction zones incorporating restriction enzymes; integrated devices combining the above reaction zones with a hydrophilic-matrix separation column to analyze reaction components, FIG 6 shows another embodiment of the invention.[.] This device is configured as an array of electrokinetic pumps for transport of a sample solution through an array of reaction zones. In this device a hydrophilic-matrix conductor 2 is deposited onto a planar insulating substrate with integral electrodes 7a and 7b. The hydrophilic matrix is formed as a parallel array of branch elements joining at a common reservoir 2b. Conductors and reservoir are coated with a cover layer 3 of a water vapor-permeable insulator. The device has an array of openings 4 for influx of a sample solution into the hydrophilic-matrix conductor 2. There is one opening 4 in each of the conductor branches. A reaction zone 6 is provided at each opening.

In a specific example of the device of FIG. 6 the reaction zones 6 contain immobilized binding [ligands] molecules. Thus, this embodiment now provides ligand binding arrays and their processes for the manufacture. Such devices are very familiar in the fields of immunoassay and DNA hybridization probes with the added benefit that each element of the binding array can have the sample solution electrokinetically pumped to it under device control. In operation, a portion of the top surface of the device is immersed in a sample solution containing one or more species for assay. As in the previous embodiments of this invention, water 50 is transported as its vapor into the hydrophilic matrix. Once wet-up the activated hydrophilic matrix becomes a conducting electrolyte. Electrokinetic transport occurs when a voltage is applied to the electrodes 7a and 7b. In this embodiment it is preferable that the hydrophilic matrix be chosen with a large

electroosmotic coefficient such that electroosmosis of the entire solution is the fastest transport mode. The purpose of the electrokinetic pump is to transport target molecules from the bulk sample solution to the reaction zone containing ligand where they are bound and detected. Electrokinetic transport of sample solution containing target molecules to the binding site enhances the speed and sensitivity of the ligand-binding reaction compared to the standard ligand-binding array where the target molecules diffuse from the bulk solution to the binding site.

Each of the reaction zones 6 of the FIG. 6 embodiment can contain a different binding [ligand] molecule as is typical of ligand-binding arrays. In a variation of the FIG. 6 embodiment it is also possible to configure a separate electrode for each of the branch elements of the hydrophilic matrix 2. In this way there is additional flexibility to apply different voltages for each branch, or to regulate the timing at which each pump is activated. Those skilled in the art will recognize that there can be different arrangements of the location of pumping electrodes relative to openings 4 and reaction zones 6 that will also achieve the desired object of electrokinetically pumping a test solution through the reaction zone. For example the opening could be located over a hydrophilic matrix conductor between the integral pumping electrodes. Also, one of the electrokinetic-pump electrodes could be immersed in, and in contact with the sample solution. Non-integral electrodes immersed in aqueous reservoirs connected to the sample solution and reservoir 2b also could provide the electrokinetic pump's power. The detailed position of the ligand-binding elements 6 relative to the orifices 4 and conductor 2 maybe somewhat different from the schematic of FIG. 6. Orifices 4 may be located at an end location of the conduit as in the embodiment of FIG. 1. Instead of locating the ligand-binding